# PREPARE: the prevalence of perioperative anaemia and need for patient blood management in elective orthopaedic surgery: A multicentre, observational study

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Abstract: BACKGROUND Patient blood management (PBM) can prevent preoperative anaemia, but little is known about practice in Europe. OBJECTIVE To assess the pre and postoperative prevalence and perioperative management of anaemia in patients undergoing elective orthopaedic surgery in Europe. DESIGN An observational study; data were collected from patient records via electronic case report forms. SETTING Seventeen centres in six European countries. Centres were stratified according to whether they had a PBM programme or not. PATIENTS One thousand five hundred and thirty-four patients undergoing major elective hip, knee or spine surgery [49.9% hip, 37.2% knee, 13.0% spine; age 64.0 years (range 18 to 80), 61.3% female]. MAIN OUTCOME MEASURES Prevalence of preoperative (primary endpoint) and postoperative anaemia [haemoglobin (Hb) <13 g dl (male), Hb <12 g dl (female)], perioperative anaemia management, time to first blood transfusion and number of transfused units. Data are shown as mean (SD) or median (interquartile range). RESULTS Anaemia prevalence increased from 14.1% preoperatively to 85.8% postoperatively. Mean Hb decrease was 1.9 (1.5) and 3.0 (1.3) g dl in preoperatively anaemic and nonanaemic patients, respectively ($P < 0.001$). In PBM ($n = 7$) vs. non-PBM centres, preoperative anaemia was less frequent (8.0 vs. 18.5%; $P < 0.001$) and iron status was assessed more frequently (ferritin 11.0 vs. 2.6%, transferrin saturation 11.0 vs. 0.1%; $P < 0.001$). Perioperative anaemia correction (mainly transfusion) was given to 34.3%. Intraoperatively, 14.8% of preoperatively anaemic and 2.8% of nonanaemic patients received transfusions [units per patient: 2.4 (1.5) and 2.2 (1.4), median time to first intraoperative transfusion: 130 (88, 158) vs. 179 (135, 256) min; $P < 0.001$]. Postoperative complications were more frequent in preoperatively anaemic vs. nonanaemic patients (36.9 vs. 22.2%; $P = 0.009$). CONCLUSION Most patients who underwent elective orthopaedic surgery had normal preoperative Hb levels but became anaemic after the procedure. Those who were anaemic prior to surgery had an increased intraoperative transfusion risk and postoperative complication rate. PBM measures such as iron status assessment and strategies to avoid transfusion are still underused in Europe.

DOI: https://doi.org/10.1097/EJA.0000000000000202

management in elective orthopaedic surgery: A multicentre, observational study. European Journal of Anaesthesiology, 32(3):160-167.
DOI: https://doi.org/10.1097/EJA.0000000000000202

EJA

*Eur J Anaesthesiol* 2015; **32:**160–167

ORIGINAL ARTICLE

# PREPARE: the prevalence of perioperative anaemia and need for patient blood management in elective orthopaedic surgery

## *A multicentre, observational study*

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**BACKGROUND** Patient blood management (PBM) can prevent preoperative anaemia, but little is known about practice in Europe.

**OBJECTIVE** To assess the pre and postoperative prevalence and perioperative management of anaemia in patients undergoing elective orthopaedic surgery in Europe.

**DESIGN** An observational study; data were collected from patient records via electronic case report forms.

**SETTING** Seventeen centres in six European countries. Centres were stratified according to whether they had a PBM programme or not.

**PATIENTS** One thousand five hundred and thirty-four patients undergoing major elective hip, knee or spine surgery [49.9% hip, 37.2% knee, 13.0% spine; age 64.0 years (range 18 to 80), 61.3% female].

**MAIN OUTCOME MEASURES** Prevalence of preoperative (primary endpoint) and postoperative anaemia [haemoglobin (Hb) $<13\,g\,dl^{-1}$ (male), Hb $<12\,g\,dl^{-1}$ (female)], perioperative anaemia management, time to first blood transfusion and number of transfused units. Data are shown as mean (SD) or median (interquartile range).

**RESULTS** Anaemia prevalence increased from 14.1% preoperatively to 85.8% postoperatively. Mean Hb decrease was 1.9 (1.5) and 3.0 (1.3) $g\,dl^{-1}$ in preoperatively anaemic and nonanaemic patients, respectively ($P<0.001$). In PBM ($n=7$) vs. non-PBM centres, preoperative anaemia was less frequent (8.0 vs. 18.5%; $P<0.001$) and iron status was assessed more frequently (ferritin 11.0 vs. 2.6%, transferrin saturation 11.0 vs. 0.1%; $P<0.001$). Perioperative anaemia correction (mainly transfusion) was given to 34.3%. Intraoperatively, 14.8% of preoperatively anaemic and 2.8% of nonanaemic patients received transfusions [units per patient: 2.4 (1.5) and 2.2 (1.4), median time to first intraoperative transfusion: 130 (88, 158) vs. 179 (135, 256) min; $P<0.001$]. Postoperative complications were more frequent in preoperatively anaemic vs. nonanaemic patients (36.9 vs. 22.2%; $P=0.009$).

**CONCLUSION** Most patients who underwent elective orthopaedic surgery had normal preoperative Hb levels but became anaemic after the procedure. Those who were anaemic prior to surgery had an increased intraoperative transfusion risk and postoperative complication rate. PBM measures such as iron status assessment and strategies to avoid transfusion are still underused in Europe.

**Published online 6 January 2015**

## Introduction

Preoperative anaemia is a common condition among patients undergoing elective surgery.[1–3] Depending on the cohort under investigation, the reported prevalences reach up to 75%[4] and in orthopaedic surgery range from 7 to 35%.[5,6] Preoperative anaemia is associated with an increased risk of postoperative morbidity[1,7–10] and

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DOI:10.1097/EJA.0000000000000202

mortality[1,3,11–13] as well as prolonged hospital stay.[3,8,13] In addition, preoperatively anaemic patients are more likely to receive perioperative red blood cell (RBC) transfusions than nonanaemic patients.[4,9,11,14] Hip and knee arthroplasties are among the surgical procedures most commonly associated with RBC transfusions.[2]

Analyses of large numbers of surgical patients showed a dose-dependent association between RBC transfusion and adverse outcomes such as increased mortality, morbidity and sepsis.[15–17] A Cochrane review of 19 randomised controlled studies comparing restrictive vs. liberal transfusion strategies in 6264 patients showed that the restricted use of RBC transfusions had no adverse influence on functional recovery or length of hospital stay.[18] Restrictive transfusion strategies were associated with a statistically significant reduction in hospital mortality and a numerical reduction in 30-day mortality that was close to being statistically significant. Interestingly, one trial in critically ill patients showed a significant association between restricted transfusion and lower mortality rates among subgroups with less severe conditions (APACHE II score $\leq$20) and lower age (<55 years).[19] Overall, the available data suggest that rather than being a first-line anaemia treatment, RBC transfusions should be the last resort.[20,21] An approach that is intended to reduce RBC transfusion is called patient blood management (PBM) and is based on three pillars: correction of preoperative anaemia, reduction of perioperative blood loss and managing iron status.[2,21,22]

The implementation of PBM has resulted in better postsurgical outcome and considerable financial savings.[23–26] Recently, an expert panel, and the European Society of Anaesthesiology, have both underscored the need for preoperative evaluation and treatment of anaemia.[23,27] The need to implement PBM is also being increasingly recognised by clinicians; yet little is known about its penetration into European centres.[28] This observational study assessed the pre and postoperative prevalence and management of anaemia in patients undergoing elective orthopaedic surgery in Europe.

## Materials and methods

### Study design and patients

This study was designed as an observational, multicentre study across six European countries. According to local legislation, the study protocol, any protocol amendments and the patient consent form were submitted to institutional review boards and ethics committees for review and approval. The study was conducted in compliance with the International Conference on Harmonisation of Good Clinical Practice and all applicable local and national guidelines and regulations. From November 2010 to March 2011, trained medical staff collected anonymised data on patient and treatment characteristics, haematological and laboratory test results, as well as treatment outcomes and complications from patient records via electronic case report forms. All collected data were subject to a plausibility and quality check. Entries that did not pass the plausibility and quality check were verified by phone interviews.

Up to 100 patients per centre, who consecutively completed elective orthopaedic hip, knee or spine surgery between 1 January 2010 and 1 July 2010, were included in reverse chronological order of the date of completing the surgical procedure. Eligible patients were 18 to 80 years of age, had a preoperative assessment within 1 day to 6 weeks prior to surgery, at least one pre and one postoperative haemoglobin (Hb) level (maximum 4 weeks after surgery) available and provided written informed consent if required by local regulations. Patients would have been excluded from participation if surgery was an emergency (no time for preoperative anaemia management), if the procedure was outside the scope of this study, if they were pregnant at the time of surgery and if there was a history of major surgical intervention within 4 weeks prior to the elective orthopaedic procedure.

Participation did not require any additional visits or assessments. The administration of RBC transfusion followed institutional policies. Centres with an institutional, preoperative erythropoietin or iron treatment protocol to treat or prevent preoperative anaemia were considered as a PBM centre. Use of antifibrinolytics was not recorded.

### Objectives

Primary endpoint was the prevalence of preoperative anaemia according to the WHO criteria [Hb <13 g dl$^{-1}$ (male), Hb <12 g dl$^{-1}$ (female)] in patients undergoing elective orthopaedic surgery. Secondary endpoints were patient outcomes such as prevalence of postoperative anaemia, transfused RBC volume and time to the first RBC transfusion (exclusive of the use of cell saver blood), length of stay (LOS) as well as perioperative anaemia treatment regimens used. In addition, the incidence of postoperative complications such as deep vein thrombosis, pulmonary embolism, bleeding, myocardial infarction/ischaemia, arrhythmia, stroke, hypotension, urinary tract infection, renal failure, wound infection, sepsis and laboratory abnormalities (other than electrolyte disturbances) were recorded using site-specific definitions. Adverse drug reactions and serious adverse events were not recorded.

Blood loss was calculated from pre and postoperative haematocrit (HCT) values, intraoperatively administered transfusion volume ($V_{Tx}$ in litres) and estimated blood volume according to the following formula:[29]

$$BL = 2 * (BV * HCT_{pre} - BV * HCT_{post} + V_{Tx} * HCT_{Tx}) * (HCT_{pre} + HCT_{post})^{-1}$$

BV = a + b*preop-weight (kg) $1000^{-1}$; (for males a = 1530 and b = 41, for females a = 864 and b = 47.9).

### Statistical methods

The proposed sample size of 1100 to 1500 patients was based on assumptions[30] about minimum differences found between preoperatively anaemic and nonanaemic patients, with a power of more than 90% and two-sided alpha of 5%. On the basis of the results of a systematic review,[2] minimum detectable differences for patients transfused, the number of RBC units given and LOS was set to 9.9%, 0.7 RBC units and 1.0 days, respectively.

Descriptive statistical analysis summarised continuous data by mean (standard deviation, SD), median with 25 and 75% quartiles (Q1, Q3) as appropriate or minimum and maximum values. Categorical data were summarised by the number and percentage of individuals in each category. Analysis of variance (ANOVA) or analysis of covariance (ANCOVA) was used for comparison of continuous data and logistic regression was used for categorical data (SAS version 9.3; SAS Inc., Cary, North Carolina, USA). Missing data were treated as missing.

Multivariate models were conducted using age, sex, American Society of Anesthesiologists (ASA) Physical Status class, anaemic status, transfusion type, surgical procedure, enrolment in a PBM centre and the interaction between PBM centre and transfusion type as covariates. Only covariates remaining statistically significant at a level of 5% (i.e. age, transfusion type and enrolment in a PBM centre) were kept in the final model. Normality of the distribution of the data was explored using the Shapiro–Wilk test and by mean of distribution plots. Sensitivity analyses were conducted by excluding extreme values and applying log-transformation in order to confirm the results of the main analysis.

## Results

### Patient characteristics

Data from all 1534 screened patient records who underwent elective orthopaedic surgery of the hip (765, 49.9%), knee (570, 37.2%) or spine (199, 13.0%) in 17 centres in six countries (Austria, France, Germany, The Netherlands, Spain and UK) were collected and analysed (Table 1). Mean age of patients was 64.0 years and 938 (61.3%) were female. Baseline (preoperative) SBP and DBP were comparable for preoperatively anaemic and nonanaemic patients. Seven (41%) of the 17 centres that enrolled 635 (41.4%) patients were considered as PBM centres.

### Anaemia prevalence

Prior to surgery, 217 (14.1%) patients were anaemic (Fig. 1) and this proportion increased to 1315 (85.8%) postoperatively. The prevalence of preoperative anaemia was comparable in patients for hip and knee surgery (12.9 and 13.2%, respectively) but higher in patients undergoing surgery of the spine (21.6%; $P = 0.001$ vs. hip and knee combined). No patient had a preoperative Hb level less than 8 g dl$^{-1}$. Postoperatively, the prevalence of Hb less than 8 g dl$_{-1}$ was 13.9% among preoperatively anaemic and 2.1% among nonanaemic preoperative patients ($P < 0.001$) (overall 3.7%). The median time between the last preoperative Hb assessment and surgery was 1 day (1 to 15) for preoperatively anaemic and 7 days (1 to 25) for nonanaemic preoperative patients ($P < 0.001$). Postoperatively, 83.8% of nonanaemic preoperative patients became anaemic and 97.7% of preoperatively anaemic patients remained anaemic ($P < 0.001$). In PBM centres, the prevalence of preoperative anaemia was lower than in non-PBM centres (8.0 vs. 18.5%; $P < 0.001$), whereas the prevalence of postoperative anaemia was similar (84.3 vs. 86.8%; $P = 0.249$). The prevalence of postoperative Hb levels less than 8 g dl$^{-1}$ was lower in PBM than in non-PBM centres (overall 1.4 vs. 5.3%, $P < 0.001$; preoperatively anaemic patients 17.0 vs. 3.9%, $P < 0.019$).

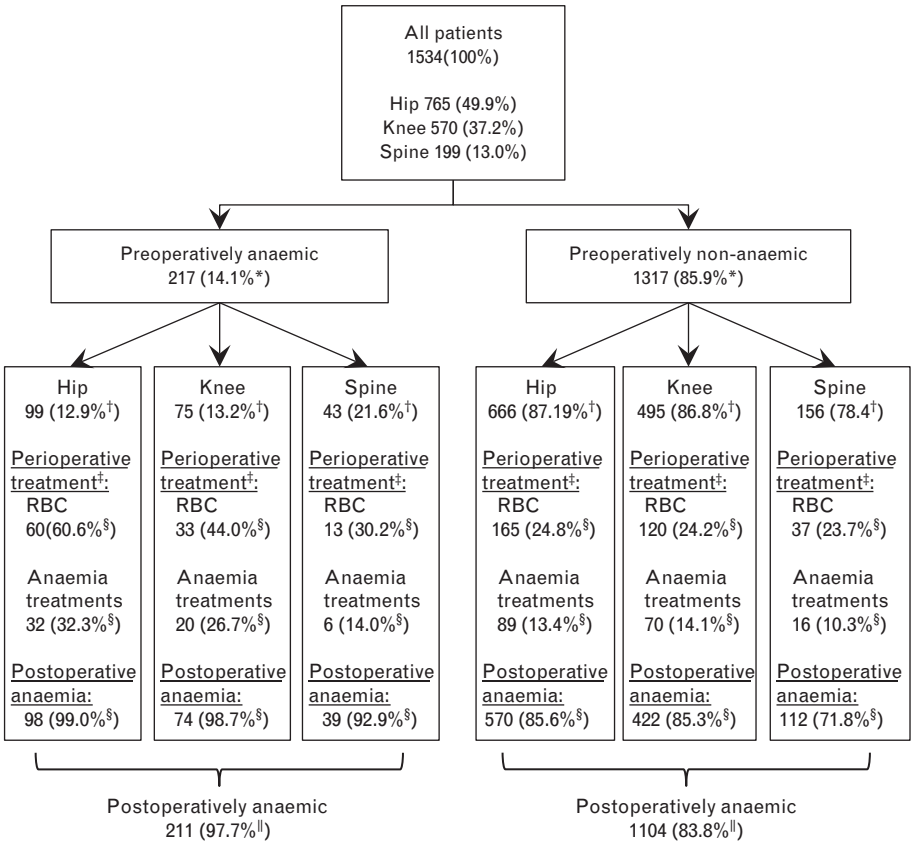
Mean fall in Hb was larger in nonanaemic preoperative patients [−3.0 (1.3) g dl$^{-1}$] than in preoperatively anaemic patients [−1.9 (1.5) g dl$^{-1}$; $P < 0.001$; adjusted for procedure and sex]. Overall, mean Hb levels decreased

**Table 1 Patient baseline characteristics**

| | All | Type of surgery Hip | Knee | Spine |
|---|---|---|---|---|
| Number of patients, *n* (%) | 1534 (100) | 765 (49.9) | 570 (37.2) | 199 (13.0) |
| Age (years) | 64.0 ± 12.3 | 63.7 ± 12.3 | 67.1 ± 8.9 | 56.0 ± 16.2 |
| female, % | 61.3 | 58.4 | 67.2 | 55.8 |
| Weight (kg) | 79.7 ± 16.3 | 78.3 ± 15.5 | 83.3 ± 16.9 | 74.9 ± 15.9 |
| Preoperative Hb (g dl$^{-1}$) | 13.7 ± 1.5 | 13.8 ± 1.5 | 13.6 ± 1.3 | 13.7 ± 1.6 |
| Serum ferritin (ng ml$^{-1}$) (tested patients, *n*) | 106 ± 108 (93) | 144 ± 166 (26) | 87 ± 65 (54) | 108 ± 91 (13) |
| Transferrin saturation (TSAT), % (tested patients, *n*[a]) | 29.2 ± 9.9 (71) | 30.1 ± 11.1 (22) | 28.1 ± 8.8 (39) | 31.7 ± 11.8 (10) |
| Anaesthetic risk assessment (according to ASA classification), % | | | | |
| ASA 1 | 13.5 | 13.7 | 11.3 | 19.2 |
| ASA 2 | 65.0 | 67.1 | 67.7 | 48.3 |
| ASA 3 | 20.7 | 18.2 | 20.2 | 32.0 |
| ASA 4 | 0.8 | 0.9 | 0.8 | 0.6 |

Data shown as % of all patients or mean ± SD; Hb, haemoglobin. [a]TSAT was tested in 6 (2.8%) of preoperatively anaemic and 65 (4.9%) of nonanaemic patients.

**Fig. 1**




Prevalence of pre and postoperative anaemia and incidence of perioperative anaemia treatment by site of surgery (see Table 2 for split of perioperative anaemia treatment into type of treatment and phase of administration).

from 13.7 (1.5) g dl$^{-1}$ preoperatively to 10.8 (1.6) g dl$^{-1}$ postoperatively ($P < 0.001$) without significant differences between the different procedures. Mean Hb change was −2.9 (1.4) g dl$^{-1}$ overall and similar in PBM and non-PBM centres [−2.9 (1.4) and − 2.8 (1.4) g dl$^{-1}$, respectively]. Calculated blood loss was 1.68 l (range 0.07 to 7.83 l) in nonanaemic preoperative patients and 1.93 l (0.07 to 12.27 l) in those anaemic preoperatively ($P = 0.016$).

### Postoperative outcomes

Preoperatively anaemic patients experienced a higher rate of postoperative complications (36.9 vs. *22.2%*; $P = 0.009$) and a longer hospital stay (11.7 ± 9.6 vs. 8.8 ± 5.9 days; $P < 0.001$) than those with no preoperative anaemia, which is in accord with a higher rate of ASA scores 3 to 4 among preoperatively anaemic vs. nonanaemic patients (35.1 and 18.4%, respectively). Multivariate analyses after adjustment for sex, age, ASA and preoperative anaemia status showed that LOS is independently associated with receipt of a RBC transfusion and enrolment in a non-PBM centre (Table 2). Also, patients who had received a RBC transfusion and were adjusted for ASA and surgical procedure had a higher risk of postoperative complications than patients without RBC transfusions (Table 2). Overall, excluding electrolyte disturbances, hypotension, vomiting, bleeding and urinary retention, the most common postoperative complications were laboratory abnormalities (Table 3).

### Assessment of iron status and inflammation

Iron status was only assessed in a small percentage (<10%) of patients. Serum ferritin was assessed in 93 patients (6%) overall, with a higher rate in PBM vs. non-PBM centres [$n = 70$ (11.0%) vs. $n = 23$ (2.6%); $P < 0.001$]. Preoperative mean serum ferritin levels were similar between PBM and non-PBM centres [100 (108) vs. 124 (110) ng ml$^{-1}$; $P = 0.36$] and between anaemic [$n = 12$ (5.5%)] and nonanaemic [$n = 81$ (6.2%)] patients [104 (90) vs. 106 (111) ng ml$^{-1}$; $P = 0.946$]. Among nonanaemic preoperative patients with available ferritin levels who became anaemic after surgery, 47 (61.8%) had preoperative serum ferritin levels less than 100 ng ml$_{-1}$, indicating iron deficiency.[1] Preoperative transferrin saturation

**Table 2 Association of length of stay and postoperative complications with red blood cell transfusion and enrolment in a nonpatient blood management centre**

| Multivariate analyses (adjusted for sex, age, ASA and preoperative anaemia status) | mean difference [95% CI]; *P* |
|---|---|
| LOS associated RBC vs. no RBC transfusion | 2.07 [0.58 to 3.56]; $P=0.007$ ($n=1372$) |
| LOS associated with non-PBM vs. PBM centre | 1.88 [0.38 to 3.38]; $P=0.014$ ($n=1372$) |
| RBC-transfused patients (adjusted for ASA and surgical procedure) | Odds ratio [95% CI] |
| Postoperative complications in patients with | |
| Allogeneic vs. no RBC | 3.2 [2.3 to 4.5] ($n=1381$) |
| Autologous vs. no RBC | 1.5 [1.0 to 2.3] ($n=1381$) |

CI, confidence interval; LOS, length of stay; PBM, patient blood management; RBC, red blood cell.

(TSAT) was almost exclusively assessed in PBM centres [$n=70$ (11.0%) vs. $n=1$ (0.1%); $P<0.001$]. TSAT was lower in preoperatively anaemic [20.9 (11.3)%; $n=6$] than in nonanaemic patients [30.0 (9.5)%; $n=65$; $P=0.031$].

C-reactive protein (CRP) was assessed in 364 (27.6%) of nonanaemic preoperative patients and 62 (28.6%) of anaemic patients. Median CRP levels were 0.26 (0.10 to 0.51) and 0.49 (0.20 to 1.77) $g\,l^{-1}$, respectively (maximum levels 6.78 and 24.8 $g\,l^{-1}$).

### Anaemia management

Perioperative anaemia was treated in 131 (60.4%) of preoperatively anaemic and 395 (30.0%) nonanaemic preoperative patients [$P<0.0001$; overall 526 (34.3%), Fig. 1, Table 4]. Anaemia treatment predominantly consisted of RBC transfusion [267 (50.8%) allogeneic, 161 (30.6%) autologous (% of treated patients)] followed by iron supplementation [127 (24.1%) oral, 74 (14.1%) intravenous iron]. The use of erythropoiesis-stimulating agents (ESAs) was uncommon (overall 1.4% of all patients). Allogeneic RBC transfusion and oral iron were more frequently used for preoperative anaemia than in patients not anaemic preoperatively ($P<0.001$). The use of autologous RBC transfusion was similar in preoperatively anaemic and nonanaemic patients ($P=0.416$).

Blood from cell salvage procedures was used in 152 (9.9%) patients overall, with comparable rates among those with allogeneic or without RBC transfusion (6.0 and 9.0%, respectively; $P=0.132$). Among the 161 patients receiving autologous RBC transfusion, 35 (21.7%) also received cell salvage blood ($P<0.0001$ vs. patients with nonautologous RBC transfusion). The majority of transfused patients received at least 2 RBC units and the mean number of units per patient was similar, although statistically different between preoperatively anaemic and nonanaemic patients [2.4 (1.5) vs. 2.2 (1.4) units, $P<0.001$]. Median (Q1, Q3) time to first intraoperative RBC transfusion (excluding cell saver blood) was 130 min (88, 158) in anaemic compared with 179 min (135, 256) in nonanaemic patients ($P<0.001$; adjusted by procedure).

The percentage of patients who had received a RBC transfusion varied considerably across participating centres. In non-PBM centres, more patients received allogeneic RBC transfusions than in PBM centres (21.2 vs. 11.7%; $P<0.001$, Table 4), whereas the use of autologous RBC transfusion was comparable (10.8 vs. 10.1%; $P=0.487$). Overall, patients with knee surgery had the lowest rate of transfusion during surgery (2.1%) compared with 4.7% and 10.6% among patients undergoing hip or spine procedures, respectively.

## Discussion

This observational study has shown that a relatively low proportion of patients (14.1%) present with preoperative anaemia but a very much higher proportion (85.7%) become anaemic after elective major orthopaedic surgery. Overall, patients experienced a mean decrease in Hb levels of 2.9 $g\,dl^{-1}$, which probably translated into

**Table 3 Postoperative complications in the overall population and stratified by preoperative anaemia status and type of centre (patient blood management vs. nonpatient blood management centre)**

| Type of complication[a] | Overall ($n=1534$) | Preoperative anaemia ($n=217$) | No preoperative anaemia ($n=1317$) | PBM centre ($n=899$) | Non-PBM centre ($n=635$) |
|---|---|---|---|---|---|
| Total | 372 (24.3) | 80 (36.9%) | 292 (22.2%) | 136 (21.4%) | 236 (26.3%) |
| Laboratory abnormality[b] | 113 (7.4%) | 25 (11.5%) | 88 (6.7%) | 6 (0.9%) | 107 (11.9%) |
| Hypotension | 71 (4.6%) | 17 (7.8%) | 54 (4.1%) | 19 (3.0%) | 52 (5.8%) |
| Vomiting | 50 (3.3%) | 9 (4.1%) | 41 (3.1%) | 27 (4.3%) | 23 (2.6%) |
| Bleeding | 41 (2.7%) | 14 (6.5% | 27 (2.1%) | 21 (3.3%) | 20 (2.2%) |
| Urinary retention | 28 (1.8%) | 3 (1.4) | 25 (1.9%) | 23 (3.6%) | 5 (0.6%) |
| Wound infection | 24 (1.6%) | 8 (3.7%) | 16 (1.2%) | 7 (1.1%) | 17 (1.9%) |
| Oliguria | 21 (1.4%) | 8 (3.7%) | 13 (1.0%) | 8 (1.3%) | 13 (1.4%) |
| Confusion | 17 (1.1%) | 5 (2.3%) | 12 (0.9%) | 6 (0.9%) | 11 (1.2%) |
| Surgical failure Repeat surgery | 15 (1.0%) | 6 (2.8%) | 9 (0.7%) | 5 (0.8%) | 10 (1.1%) |

Data are shown as number of patients and percentage of the respective subgroup. No statistical tests of subcategories have been performed, as the small numbers do not permit reliable subanalyses. PBM, patient blood management. [a] Reported for more than 2% of any population. [b] Other than electrolyte disturbance.

**Table 4** Perioperative anaemia management by preoperative anaemia status and type of centre (patient blood management vs. nonpatient blood management centre). More than one treatment per patient was possible[a]

| | Patients total (*n*) | Patients with anaemia treatment* (%) | | | | |
|---|---|---|---|---|---|---|
| | | RBC transfusion | | | | |
| | | Autologous | Allogeneic | Oral iron | i.v. iron | ESA |
| Perioperative | 1534 | 10.5% | 17.4% | 8.3% | 4.8% | 1.4% |
| Anaemic[a] | 217 | 10.1% | 38.7% | 16.6% | 4.1% | 3.7% |
| Nonanaemic[a] | 1317 | 10.6% | 13.9% | 6.9% | 4.9% | 1.1% |
| PBM centre | 635 | 9.8% | 11.3% | 6.9% | 5.5% | 2.5% |
| Non-PBM centre | 899 | 11.0% | 21.7% | 9.2% | 4.3% | 0.7% |
| Preoperative | 1534 | 0.2% | 0.2% | 2.3% | 0.8% | 1.4% |
| Anaemic[a] | 217 | 0.5% | 0.5% | 6.0% | 1.8% | 3.2% |
| Nonanaemic[a] | 1317 | 0.2% | 0.2% | 1.7% | 0.6% | 1.1% |
| PBM centre | 635 | 0.2% | 0.2% | 2.8% | 1.7% | 2.5% |
| Non-PBM centre | 899 | 0.2% | 0.2% | 2.0% | 0.1% | 0.5% |
| Intraoperative | 1534 | 8.7% | 5.7% | 0.0% | 2.3% | 0.6% |
| Anaemic[a] | 217 | 6.0% | 16.1% | 0.0% | 1.4% | 1.8% |
| Nonanaemic[a] | 1317 | 9.2% | 4.0% | 0.0% | 2.5% | 0.4% |
| PBM centre | 635 | 8.3% | 3.5% | 0.0% | 1.3% | 0.6% |
| Non-PBM centre | 899 | 9.0% | 7.3% | 0.0% | 3.1% | 0.5% |
| Postoperative | 1534 | 1.8% | 13.8% | 7.6% | 2.4% | 0.5% |
| Anaemic[a] | 217 | 3.7% | 30.9% | 15.7% | 0.9% | 1.8% |
| Nonanaemic[a] | 1317 | 1.5% | 10.9% | 6.3% | 2.7% | 0.2% |
| PBM centre | 635 | 1.4% | 9.3% | 5.5% | 4.1% | 0.2% |
| Non-PBM centre | 899 | 2.1% | 16.9% | 9.1% | 1.2% | 0.7% |

*patients could have received more than one treatment; [a]preoperative anaemia status i.v., intravenous; PBM, patient blood management; RBC, red blood cell.

the high rate of postoperative anaemia. Notably, a considerable proportion of patients became severely anaemic (Hb $<8\,g\,dl^{-1}$) after surgery with a higher prevalence in non-PBM than in PBM centres, and particularly among those who were already anaemic (17.0%). Together with the finding that PBM measures are underused, the high rate of postoperative anaemia underscores the need for effective PBM that goes beyond treating preoperative anaemia to include reducing intraoperative blood loss and immediate postoperative anaemia, and managing iron status.

The observed prevalence of preoperative anaemia in our study compares with the findings in reported studies in orthopaedic surgery (7 to 35%).[5,6] The prevalence of postoperative anaemia is also in the range reported for hip fracture surgery (74 to 93%)[2] and hip or knee arthroplasty (95%).[31] Given the drop in Hb when comparing pre and postoperative values, a blood loss calculation was performed on the basis of measured haematocrit values and administered RBC transfusion. The high calculated blood loss values are in line with the high rate of postoperative anaemia despite a rather low prevalence of preoperative anaemia in this patient group.

Statistical analysis of data from the entire cohort suggests an association between preoperative anaemia, a higher rate of postoperative complications and also a longer hospital stay. This association probably reflects the more severe underlying conditions that are indicated by higher ASA scores among the preoperatively anaemic patients. However, the correlation between LOS, receipt of a RBC transfusion and admission to a non-PBM centre remained after adjustment for ASA, preoperative anaemia status and also sex and age. The immediate pretransfusion Hb levels have not been recorded and so we cannot verify whether differences in transfusion rates correlate with different Hb levels, as transfusion triggers vary across centres. Nevertheless, these findings are in line with previous publications[7–10] and corroborate the results of a recent study by Musallam *et al.*,[1] which analysed database entries from 227 425 patients undergoing noncardiac surgery. In this study, perioperative transfusion in itself was found to be associated with increased mortality and morbidity. Furthermore, the prevalence of preoperative anaemia was 30.4%, with anaemia being independently and significantly associated with increased 30-day morbidity. Data from our audit complement the findings by Musallam *et al.*[1] by providing detailed insights into the defined subgroup of elective orthopaedic surgery patients, additionally including data on pre, intraoperative and postoperative anaemia management and assessment of iron status.

Despite recommendations that were published long before the patients in this study underwent surgery,[32] the percentage assessed for iron status in the preoperative period was very low (<10%) and consistent with iron being underused as a treatment option. Even in PBM centres, only a minority of patients were tested for their ferritin levels or TSAT, suggesting the need for an evaluation of how PBM is actually implemented in centres claiming to be a PBM centre. Iron status assessment is not expensive and could be systematically performed in this high-risk population.

Lower TSAT in preoperatively anaemic patients may indicate the presence of iron deficiency in this subgroup. Notably, 57 patients (61.3% of tested patients) had baseline serum ferritin levels less than 100 ng ml_1 and most

of them (47 patients) became anaemic postoperatively; eight had already been anaemic preoperatively. However, we cannot evaluate the prevalence of iron deficiency in the entire study population. Interestingly, the average time between last Hb measurement and surgery was more than 1 week and was longer among nonanaemic patients. This suggests that there is time to institute preoperative anaemia management.

Notably, even among preoperatively anaemic patients, only a minority of patients received anaemia treatment such as iron or ESA. Moreover, most iron-treated patients, even those with preoperative anaemia, received oral iron despite the known limitations of oral vs. intravenous (i.v.) iron.[33,34]

Since this study, it has been shown that pre and intraoperative treatment of anaemia reduces postoperative morbidity, transfusion requirement and length of hospital stay.[23,35,36] However, considering the high estimates of postoperative anaemia in this and other studies[2,31] and the fact that iron deficiency is a main cause of anaemia,[37] appropriate iron status assessment should become part of pre and postoperative routine anaemia evaluation and management.

The high reliance on RBC transfusion is a concern. Despite continuous improvement in the production and management of RBC concentrate, there will always be a risk of transmitting new or re-emerging blood borne pathogens,[38,39] and perioperative transfusions *per se* are associated with increased morbidity and mortality even when only a single RBC unit is administered.[15,17,40] Our statistical analysis identified RBC transfusion as an independent risk factor of postoperative complications and prolonged hospitalisation (Table 2). Despite adjustment for known confounding factors, we cannot rule out that there may be additional unidentified reasons for this.

Interestingly, around 40% of RBC transfusions were autologous RBC concentrates. Furthermore, cell salvage blood was used more frequently in patients who had received autologous transfusions than in those who had received allogeneic or no transfusion. This may reflect institutional approaches towards blood conservation, as reducing blood loss and use of autologous blood salvage make up part of the second and third pillars of PBM;[22,30] yet, there were not enough data to analyse for statistical differences between centres.

Our findings indicate that PBM measures such as iron status assessment, i.v. iron treatment and erythropoietic stimulation are still underused in orthopaedic surgery in Europe. As most patients in our study became anaemic after surgery, correction of preoperative anaemia is only one important aspect of PBM. Providing patients with sufficient iron reserve to cope with the blood loss during surgery (1 ml blood corresponds approximately to 0.5 mg iron, for a 80 kg man) and addressing the impaired utilisation of iron due to chronic disease or surgery-associated activation of proinflammatory cytokines is just as important.[41,42] The benefits of postoperative i.v. iron treatment have recently been shown;[43] however, there appears to be a need to increase awareness about the role of iron in the development and treatment of anaemia, in addition to differences between oral and i.v. iron administration that can render oral iron therapy inadequate or ineffective.[44,45]

Due to the observational nature of the study, interpretation of our results is limited by the absence of a reference arm and the lack of control over the frequency and duration of treatment or the frequency of performed laboratory tests. Also, additional information about the use of antifibrinolytics might have allowed a better understanding of the high blood loss, as these agents may have influenced bleeding and transfusion requirement. On the positive side, studies such as this one reflect realities of clinical practice and show the implementation (or ignorance) of treatment recommendations and clinical evidence. Observational studies can provide the basis for new hypotheses or identify patient groups that benefit most from a certain treatment. The observed higher blood loss in preoperatively anaemic than in nonanaemic patients may have a purely mathematical explanation. As blood loss is equal to the RBC loss divided by the mean haematocrit during blood loss, the lower mean haematocrit during blood loss in preoperatively anaemic vs. nonanaemic patients (0.318 vs. 0.364; $P < 0.001$), resulted in a higher calculated blood loss. Mean RBC loss was similar in preoperatively anaemic and nonanaemic patients, respectively.

In conclusion, the results of this observational study show that most patients who underwent elective orthopaedic surgery had normal preoperative Hb levels but became anaemic after the procedure. Patients were rarely tested for their iron status and anaemia treatment was dominated by RBC transfusion despite evidence of their potential negative effects, whereas the pharmacological treatment of anaemia was underused and recent recommendations were ignored.

## Acknowledgements relating to this article

Assistance with the study: Medical writing support was provided by SFL Regulatory Affairs & Scientific Communication.

Financial support and sponsorship: This work was supported by Vifor Pharma Ltd. who sponsored the study, supported development of the study design, provided organisational and statistical support and funded medical writing support.

Conflicts of interests: S Lasocki has received speaker honoraria from Vifor Pharma and Janssen-Cilag, and served as a consultant for Vifor Pharma. R Krauspe served as consultant for Vifor Pharma. For the purpose of this study, C von Heymann has received research funding from Vifor Pharma, Janssen-Cilag and The German Red Cross, and honoraria for lectures and consultancy work from Vifor Pharma and Janssen-Cilag. A Mezzacasa and S Chainey are

employees of Vifor Pharma. DR Spahn's academic department is receiving grant support from Vifor Pharma Deutschland GmbH, Munich, Germany, Vifor Pharma Österreich GmbH, Vienna, Austria, Vifor (International) AG, St. Gallen, Switzerland.

Presentation: Data have been presented in a poster form at Euroanaesthesia 2012, 9 to 12 June, Paris, France.

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